

## REMARKS

Claims 42-58 and 60-71 are pending. Due to a restriction requirement, claims 42-52, 60, and 64-68 have been withdrawn from consideration. In the final action mailed June 29, 2010, claims 53-58, 61-63, and 69-71 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Claims 53-58, 61, 63, and 69 were rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 6,050,990 (“Tankovich”) taken in light of U.S. Patent Application Publication No. 2003/0077823 (“Li”) and PCT Publication No. WO 01/53461 (“Toma”). Claims 53-58, 61-63, and 69-71 were rejected as being obvious over Tankovich in view of Li and Toma. Each of these rejections is addressed below.

### *Claim amendments*

Claim 53 has been amended to delete “p75NTR” and “or progeny thereof.” In view of these changes, claim 70 has been cancelled. Claim 71 has been amended to depend from claim 53. These amendments add no new matter.

### *Rejection under 35 U.S.C. § 112, first paragraph*

Claims 53-58, 61-63, and 69-71 were rejected as failing to comply with the written description requirement. In making this rejection, the Office asserts that these claims lack basis in the specification for reciting that the cells do not express measurable levels of keratin 15. The Office further states that this rejection would be overcome by providing a substantive evidentiary showing by RT-PCR that SKPs do not express keratin 15.

To overcome this rejection, Applicants hereby provide RT-PCR data demonstrating that SKPs do not express keratin 15 (“Exhibit A”). As shown in this exhibit, RT-PCR performed on whole E8.5 embryos showed expression of keratin 15. By contrast, RT-PCR performed on SKPs generated no indication of keratin 15 expression.

In view of this data, withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

*Rejection under 35 U.S.C. § 102(b) or § 103(a)*

Claims 53-58, 61, 63, and 69 were rejected as being anticipated by or, in the alternative, as being obvious over Tankovich taken in light of Li and Toma. In making this rejection, the Office cites Tankovich as teaching isolating cells from skin comprising dermal papillae from a patient's own head, separating the stem cells from the skin, and grafting the cells into an incision on a desired area on said patient's own head. Applicants respectfully traverse this rejection on the grounds that Tankovich fails to teach or suggest transplanting undifferentiated stem cells and, further, fails to teach transplanting the population of cells recited in the present claims. Each of these matters is addressed below.

*Tankovich does not teach or suggest transplantation of undifferentiated stem cells*

Claim 53, as amended, requires transplantation of stem cells into the patient. Tankovich, by contrast, teaches only transplantation of *differentiated* cells. This is explained in Tankovich at column 56, lines 51-56:

The separated stem cells are then cloned by culturing them in an appropriate growth medium, such as Dulbecco's modified Eagle's medium (DMEM) with fetal calf serum, for a sufficient time to allow proliferation and differentiation of the cells.

That the cells are differentiated is further supported at column 57, lines 14-19, of Tankovich:

For interdermal grafting, the suspension of differentiated stem cells should be at a density of about 3 to about 10 percent by volume.

For grafting of the differentiated stem cells, the recipient site is prepared by scraping the skin surface and making superficial incisions of about 200 microns in depth.

For grafting of the differentiated stem cells, the recipient site is prepared by scraping the skin surface and making superficial incisions of about 200 microns in depth.

Because Tankovich neither teaches nor suggests transplantation of stem cells into a patient, this reference cannot anticipate, nor render obvious, amended claim 53 or its dependent claims.

*The stem cells isolated in Tankovich are different from those of the present application*

Tankovich does not disclose isolating and transplanting stem cells from any source other than the bulge area of the hair papilla, as explained in column 56, lines 48-49. While Tankovich notes that stem cells are present in the dermal papilla, there is no disclosure of isolating and culturing these cells and no disclosure of their use in a method of regenerating skin. In contrast to Tankovich, the stem cells of the present invention can be found in the dermal papilla (see Exhibit B) and not in the bulge area, as explained below. Thus, Tankovich cannot anticipate or render obvious the present invention.

Both the present specification and Li clearly indicate that the bulge area contains a different cell population from those recited in the present claims. This is noted in the specification at page 18, lines 6-7. Further, as explained in Example 3, the cells of the dermal papilla, in which the stem cells of claim 53 can be found, express a set of markers distinct from those found of the bulge region. Specifically, the specification at page 22, lines 20-26, notes that (references deleted, emphasis added):

At postnatal day 2, most of the maturing follicles were approaching the first synchronized anagen growth phase of the hair cycle, and low level expression of snail, slug and twist could be detected in the papillae, in addition to AP, nexin and versican. Expression of these markers did not overlap with keratin 17 expression, a marker for the bulge epidermal stem

Li also describes a different population of cells from those of claim 53. Like Tankovich, Li teaches a population of stem cells found in the bulge area. At paragraph [0013], Li identifies the bulge area as containing nestin-expressing cells:

(e) is the day 8 sample after depilation and showing the middle anagen hair follicle. Note the fully formed hair follicle with nestin-GFP expression in the upper outer-root sheath and no nestin-GFP expression in the hair follicle bulb.

Li further explains at paragraph [0014] that these nestin-expressing cells also express the epidermal marker keratin 15:

Co-localization of GFP, nestin and keratin 5/8 & 15 in hair follicle bulge stem cells and outer root sheath cells determined by immunohistochemical staining.

Note the localization on nestin-GFP and keratin-15 in the bulge hair follicle stem cells.

Based on these results, the bulge area stem cells of Li are epidermal in origin and express keratin 15. The cells of present invention, by contrast, do not express keratin 15. Thus, the cells of Li are different from those presently claimed.

Because Tankovich describes cells isolated from the same part of the hair follicle (bulge area) as those of Li, one skilled in the art would reasonably infer that Tankovich describes culture and transplantation of the cells of Li. Because the cells of Li express keratin 15, whereas the presently claimed cells do not, Li cannot support an anticipation or obviousness rejection over Tankovich.

Finally, Toma also provides no evidence to suggest that Tankovich describes transplantation of the presently claimed cells. As noted by the Office, Toma describes a peripheral stem cell population expressing nestin but not p75NTR. Toma further describes these cells as being dermal in origin, as explained on page 21. By contrast, the bulge area cells of Li express epidermal markers, including keratin 15. Toma therefore describes a population of cells distinct from those of Li. Because, as explained above,

one would conclude that Tankovich describes transplanting the cells of Li, there is no basis for concluding that the cells of Toma are the same as those described in Tankovich.

For all of these reasons, Tankovich does not describe culture and transplantation of the presently claimed cells. Withdrawal of the § 102(b) or § 103(a) rejection over Tankovich in view of Li and Toma is respectfully requested.

*Rejection under 35 U.S.C. § 103(a)*

Claims 53-58, 61-63, and 69-71 are rejected as being obvious over Tankovich in view of Li and Toma. In making this rejection, the Office cites Tankovich as teaching isolating skin comprising dermal papillae from a patient's own head, separating stem cells from the skin, cloning the cells, and grafting the cells into an incision onto a desired area of the patient's own head. The Office notes that Tankovich does not teach isolating cells that express nestin or fibronectin but not p75NTR or keratin 15. To overcome this deficiency, the Office cites Li as teaching a population of nestin-expressing stem cells in hair follicles that can regenerate skin, and Toma is cited as teaching stem cells from skin that express nestin and fibronectin, but not p75NTR. Based on these combined teachings, the Office concludes that one would reasonably infer that the cells of Tankovich express nestin and fibronectin, but not p75NTR or keratin 15. Applicants respectfully traverse.

To render a claim obvious, a reference or combination of references must teach all claim limitations. Because no combination of Tankovich, Li, and Toma teaches the use of a keratin 15 negative cell in a method of regenerating skin, these references fail to teach all claim limitations and thus cannot render claim 53 or its dependent claims obvious.

Contrary to the Office's position, there is nothing any either Li to Toma to suggest that the cells described in Tankovich do not express keratin 15. If anything, Li suggests the opposite. As explained above, Tankovich describes isolation and transplantation of stem cells from the bulge area of the hair follicle. Li, like Tankovich, also discloses stem

cells found in the bulge area and further discloses that the cells express keratin 15. Thus, based on the combined teachings of Li and Tankovich, the skilled artisan would infer that the transplanted cells of Tankovich also express keratin 15, unlike those of the present claims. For this reason, the combination of Tankovich and Li cannot render claim 53 or its dependent claims obvious.

The deficiencies of Tankovich and Li cannot be remedied by Toma. As explained above, Toma describes a dermally derived population of cells. The skilled artisan would therefore conclude that the stem cells of Toma are distinct from the keratin 15 expressing, epidermal bulge area stem cells of Li. Further, there is nothing to suggest that the cells of Toma are the same as those described in Tankovich.

Accordingly, no combination of Tankovich, Li, and Toma teach or suggest use of a nestin and fibronectin positive stem cell that does not express keratin 15 to regenerate skin, as required by the present claims. These references therefore cannot render claim 53 or its dependent claims obvious. Withdrawal of the rejection under 35 U.S.C. § 103(a) is therefore requested.

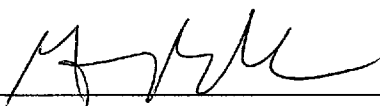
### CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. Enclosed is a Request for Continued Examination and a Petition to extend the period for replying to the final Office action for one (1) month, to and including October 29, 2010, and a check in payment of the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit  
Account No. 03-2095.

Respectfully submitted,

Date: 10/29/10

  
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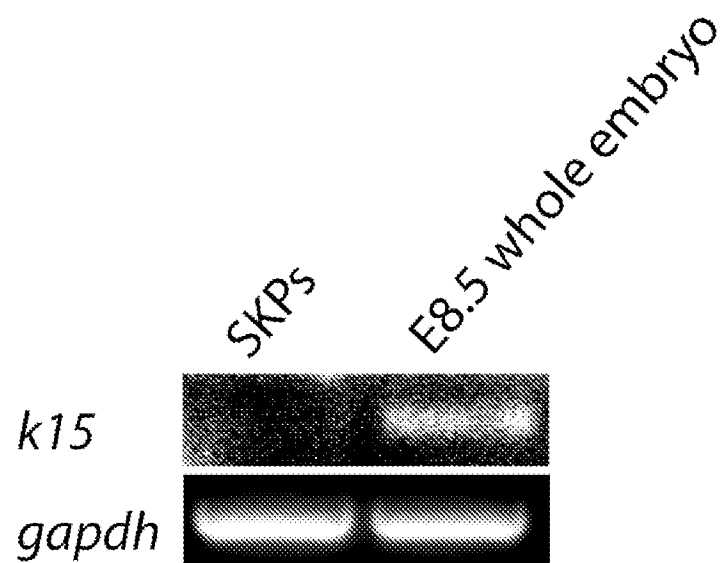
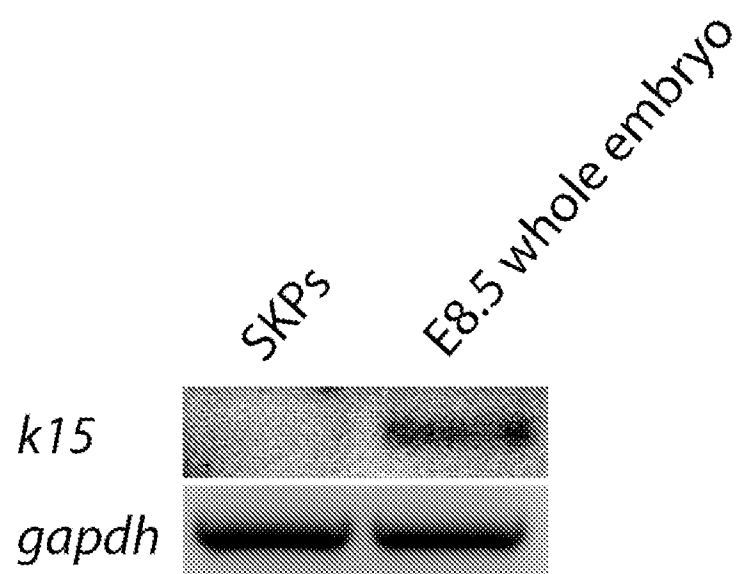
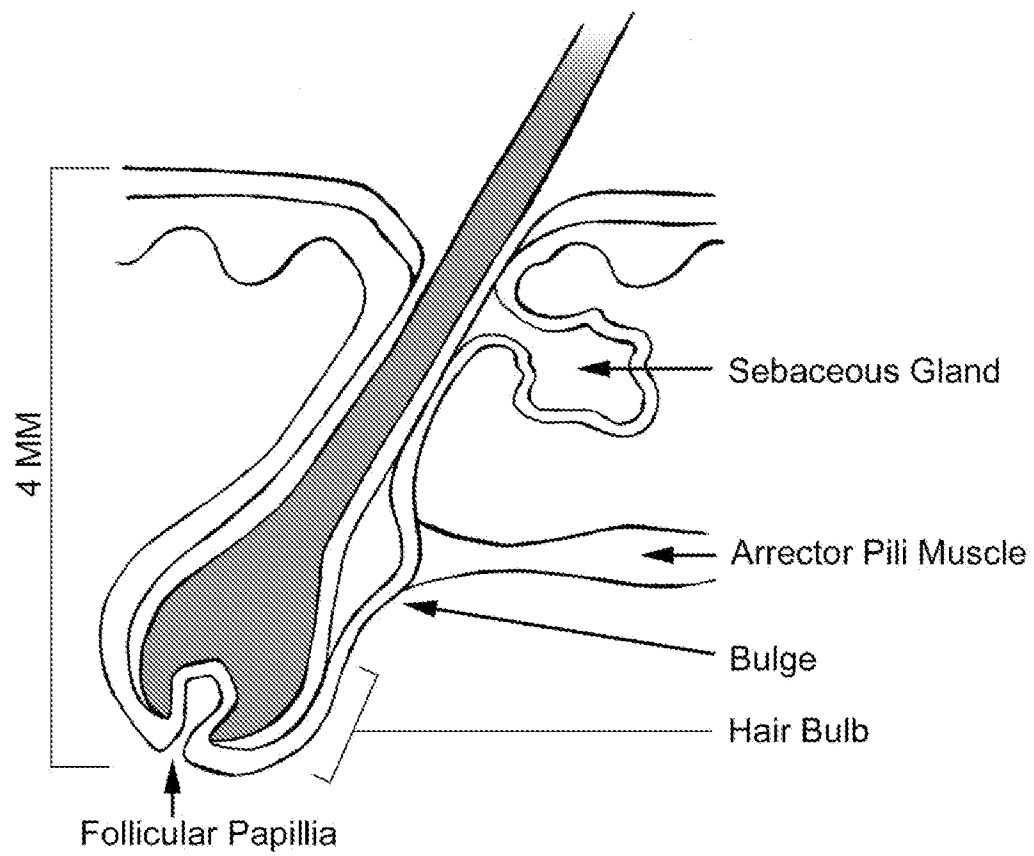


Exhibit A





**Exhibit B**